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U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER

## TRANSMITTAL LETTER TO THE UNITED STATES

MCA-483 PC/US

DESIGNATED/ELECTED OFFICE (DO/EO/US)

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR

CONCERNING A FILING UNDER 35 U.S.C. 371

Not yet assigned **10/049537**

INTERNATIONAL APPLICATION NO.

INTERNATIONAL FILING DATE

PRIORITY DATE CLAIMED

**PCT/US00/25585****18 September 2000****17 September 1999**

TITLE OF INVENTION

**HIGH THROUGHPUT SCREEN CARD**

APPLICANT(S) FOR DO/EO/US

**Brian Foley**

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (24) indicated below.
- ☐ The US has been elected by the expiration of 19 months from the priority date (Article 31).
- ☐ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
  - a. ☐ is attached hereto (required only if not communicated by the International Bureau).
  - b. ☐ has been communicated by the International Bureau.
  - c. ☒ is not required, as the application was filed in the United States Receiving Office (RO/US).
- ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
  - a. ☐ is attached hereto.
  - b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
- ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
  - a. ☐ are attached hereto (required only if not communicated by the International Bureau).
  - b. ☐ have been communicated by the International Bureau.
  - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
  - d. ☒ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).
11. ☒ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☒ A copy of the International Search Report (PCT/ISA/210).

## Items 13 to 20 below concern document(s) or information included:

13. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☒ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter.
19. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
20. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
21. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
22. ☒ Certificate of Mailing by Express Mail
23. ☒ Other items or information:

**Written opinion and response to written opinion**

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 1.445(a)(2)) <b>10/049537</b>		INTERNATIONAL APPLICATION NO. <b>PCT/US00/25585</b>		ATTORNEY'S DOCKET NUMBER <b>MCA-483 PC/US</b>	
24. The following fees are submitted: <b>BASIC NATIONAL FEE ( 37 CFR 1.492 (a) (1) - (5) ) :</b> <input type="checkbox"/> Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO ..... <b>\$1040.00</b> <input checked="" type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO ..... <b>\$890.00</b> <input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO ..... <b>\$740.00</b> <input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) ..... <b>\$710.00</b> <input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) ..... <b>\$100.00</b> <b>ENTER APPROPRIATE BASIC FEE AMOUNT =</b>				<b>CALCULATIONS PTO USE ONLY</b>	
Surcharge of <b>\$130.00</b> for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).				<b>\$0.00</b>	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	41 - 20 =	21	x \$18.00	<b>\$378.00</b>	
Independent claims	3 - 3 =	0	x \$84.00	<b>\$0.00</b>	
Multiple Dependent Claims (check if applicable). <input type="checkbox"/>				<b>\$0.00</b>	
<b>TOTAL OF ABOVE CALCULATIONS =</b>				<b>\$1,268.00</b>	
<input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27). The fees indicated above are reduced by 1/2.				<b>\$0.00</b>	
<b>SUBTOTAL =</b>				<b>\$1,268.00</b>	
Processing fee of <b>\$130.00</b> for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).				<b>\$0.00</b>	
<b>TOTAL NATIONAL FEE =</b>				<b>\$1,268.00</b>	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) (check if applicable). <input checked="" type="checkbox"/>				<b>\$40.00</b>	
<b>TOTAL FEES ENCLOSED =</b>				<b>\$1,308.00</b>	
				Amount to be: refunded	\$
				charged	\$

- a. ☐ A check in the amount of \_\_\_\_\_ to cover the above fees is enclosed.
- b. ☒ Please charge my Deposit Account No. 133577 in the amount of \$1,308.00 to cover the above fees. A duplicate copy of this sheet is enclosed.
- c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 133577. A duplicate copy of this sheet is enclosed.
- d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

**NOTE:** Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

John Dana Hubbard  
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80 Ashby Road  
Bedford, MA 01730

SIGNATURE

John Dana Hubbard

NAME

30,465

REGISTRATION NUMBER

DATE

February 7, 2002

PTO/PCT Rec'd 07 FEB 2002

10/049537

## HIGH THROUGHPUT SCREENING CARD

Inventor: Brian Foley

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This application relates to co-pending U.S. Applications "Three Dimensional Patterned Porous Structures," our reference number MCA-482 and "Patterned Porous Structures," our reference number MCA-474, both filed concurrently herewith.

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## BACKGROUND OF THE INVENTION

The Multiscreen® multiple well membrane filter for laboratory and research use, produced by Millipore Corporation, is used for laboratory assays. These filters and its competitive products are made by first creating a support plate by injection molding a resin. Typically, polyethylene, Barex™ polymer, acrylic or styrene is used as the resin. The support plate would have a number of through holes, with the wall of such holes serving as the side wall (circular well) or walls (multi-hedral well) of the wells. As such, the resin in its injection-molded form must not interfere with the laboratory assay it is used for.

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The multi-well device is then created by cutting filter membrane into discs and attaching the discs to one side of each through hole, thereby creating the wells. Such filter membrane is typically attached to the support by bonding, either thermal or ultrasonic. This is a labor-intensive operation, adding substantially to the cost of manufacturing.

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As the injection molded support plates require a mold, a mold has to be produced for each device. The process of producing a mold for use in production first requires the production of a prototype mold. Such molds cost around \$50,000. Once the final design of the product is agreed upon, a production mold is made. The cost of a production mold varies with the number of cavities intended for the injection-molding tool. For example, a one-cavity tool for 96 well plate production requires a mold that typically costs \$90,000. A two-cavity tool for 96 well plate production requires a mold that typically costs \$160,000.

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A limitation of the molds is that they are suitable only for similar materials. One could not use the polyethylene mold to produce a styrene support. This limits the products that can be made available because it is not cost effective to produce the same plate design from two different materials due to the cost of capital and the time to recoup the investment.

For example, it would be beneficial to offer a variety of materials for supports so the researcher can avoid materials that may leach extractables into their assay. Indeed, the use of Teflon® polytetrafluoroethylene ("PTFE"), a substantially inert material, is not used to produce supports because it is not a cost effective alternative for injection molding low cost parts. For example, a PTFE multi-well plate would be useful for assays that require no protein binding by the support. Indeed, a PTFE plate in combination with a low protein binding membrane would have substantial utility. Until the present invention, such a device was not available due to its cost and the limitations of technology.

The current format of choice for multi-well membrane filters is a 96 well plate with a support that is made from injection-molded resins such as polyethylene, styrene and acrylic. 12 and 24 well formats preceded the 96 well plate, but as robotics improved and sample volumes have mushroomed, the need for more assays per plate (higher well density) has increased. Moreover, the volume of the typical assay is shrinking dramatically because of the costs of the material being assayed, proteins, nucleic acids and the like, the costs of the solvents, buffers, enzymes and the like, and improvements in detection technology. As such, that market requires multiple well membrane filters that have more wells in same area with the wells having smaller volumes. Indeed, formats of 384, 1536, 9600 wells are envisioned.

Unfortunately, the injection molding process has severe limitations beyond the current 96 well format. There are substantial manufacturing hurdles with such higher density formats such as molding (more plastic, higher piece part cost, tool building and maintenance costs) and assembly (stricter tolerances are required for cutting and sealing membrane on the wells.) Moreover, the overall size of the plate cannot

expand much, if at all, due to the customers already significant sunk costs in laboratory automation.

The present invention solves the prior art problems by providing a platform suitable for affixing a membrane that results in a multi-well membrane filter suitable for high throughput screening assays in high density, low volume formats. The current invention allows for quick, inexpensive change over in the manufacturing process without the expensive tooling costs required by the injection molding process. Moreover, the present invention can provide a multi-well membrane filter that is much cheaper on a per well basis than prior art multi-well membrane filters. Lastly, the present invention provides a means for using PTFE supports in multi-well membrane filters that are competitive on a per well basis with the current injection molded polyethylene support in the 96 well format.

#### SUMMARY OF THE INVENTION

The present invention provides a multi-well membrane filter comprising a support characterized by through holes not having been molded therein; and a membrane filter fixed to said support so at least one side of at least two such through holes are covered such that the device has at least two wells suitable for receiving material to be assayed.

The present invention provides a method of producing a multi-well membrane filter device, the method comprising 1) selecting a pre-formed support suitable for affixing a membrane thereto; 2) removing material from such pre-formed support so as to form substantially aligned through holes therein; 3) selecting a membrane suitable for filtering solutions in a laboratory setting; and 4) forming wells by laminating the membrane to the support.

## BRIEF DESCRIPTION OF THE FIGURES

Figure 1 provides top and sectional views of a multi-well filter device with different well shapes and an underdrain laminated thereto

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## DETAILED DESCRIPTION OF THE SPECIFIC EMBODIMENT

The present invention provides a multi-well membrane filter, the filter comprising a support characterized by through holes not having been molded therein; and a membrane filter fixed to said support so at least one side of at least two such through  
10 holes are covered such that the device has at least two wells suitable for receiving material to be assayed.

Preferably, the support may be made of glass, metallic materials, ceramic materials, elastomeric materials and coated cellulosic materials. In a more preferable  
15 embodiment, the support includes polymeric material. Polymeric materials suitable for the present invention include polyethylene, acrylic, PTFE, polycarbonate and styrene.

Preferably, the plate height is less than 6.4 mm (one quarter inch) thick. The prior made no  
20 suggestion for the plate of the present invention because the volume requirements would have necessitated a plate of a large thickness, i.e., 12.7 mm greater than (one half inch). At such thickness, there is no motivation to using anything other than molding due to the costs of that process.

25 Preferably, the multi-well membrane filter of the present invention is configured to have at least 96 wells. In such a configuration, wells in a specific device may have different volumes. Preferably, individual wells have a volume in the range of 50 to 150 microliters. More preferably, the individual wells have a volume in the range of 70 to 130 microliters. For the 384-well format, a volume of about 100 to 120  
30 microliters is preferred. It is envisioned that for formats greater than the 384-well format, the volume requirements will diminish. The wells may also have different shapes.

In a preferred embodiment, the multi-well membrane filter of the present invention will have an underdrain laminated to the opposite side of the membrane to facilitate collection of filtrate.

- 5 In a preferred embodiment of the present invention, the membrane contains patterned porous structures.

10 The present invention provides a method of producing a multi-well membrane filter device, the method comprising selecting a pre-formed support suitable for affixing a membrane thereto; removing material from such pre-formed support so as to form substantially aligned through holes therein; selecting a membrane suitable for filtering solutions in a laboratory setting; and forming wells by laminating the membrane to the support.

- 15 Preferably, the method of the present invention includes extruding a material of -interest to form the pre-formed support.

20 Preferably, the through holes in the pre-formed support are made by selectively drilling, punching, burning or dissolving material to be removed.

25 The preferred method of laminating the membrane to the support is in a web converting process. Preferred methods of laminating include diffusion bonding, adhesive bonding, welding and thermal bonding.

30 Figure 1 provides an example of the present invention. A rigid sheet 10 is infused with a matrix of wells. The wells could be pre-punched or they could be produced online within an assembly process, such as a web converting process. For example, the perforated sheet could be presented to the assembly machine precut and stacked or on a continuous web and cut to size online. The well matrix will be determined by the end users needs, but it could have numerous configurations and the wells do not necessarily need to be all of the same shape or size. Figure 1, Top View, provides the

wells of the present invention having round, square, and other shapes. Virtually any shape that is required for the product may be provided.

The rigid sheet 10 allows for easy handling during manufacturing and easy handling during use by the end user (a human or a robot). As the web process uses sheet stock, using sheet/roll stock as the starting material allows for a variety of resins and support thicknesses because most vendors of sheet stock supply a wide range of resins and thicknesses to be used with this type of assembly process. By varying the thickness of the sheet, various products could be developed with different starting well volumes.

One could also use the same sheet thickness and vary the volume by removing more material when the through holes are created.

After the perforated sheet is produced with the appropriate array, a membrane 14 is attached to the perforated sheet. The membrane could be completely hydrophobic or hydrophilic or it could be hydrophilic with hydrophobic regions 18.

The present invention may also be used in connection with related case no. MCA-474 filed concurrently herewith that is related to porous structures having selected functional patterns upon and/or in them. That invention is particularly related to porous structures such as membranes that have a series of one or more patterns of porous and non-porous areas. Such patterned porous structures may be laminated on the support structure of the present invention. It is envisioned that non-porous regions of the membrane will be situated where the hydrophobic region 18 is in Figure 1.

A variety of laminating process is envisioned, yet the below description is not exclusive. Those of ordinary skill in the art would appreciate other means of attaching two layers together like those described herein.

The means of laminating; that is, attachment could be any of the following:

1. Heat (thermal, ultrasonic, vibration)- The membrane and perforated sheet are held together under pressure. Then ultrasonic energy, vibration energy, or thermal energy applies heat. The melted resin will be pushed into the pores of the membrane.



2. Epoxy- A very thin film of epoxy (air cured, heat cured, UV cured) is applied to 1 side of the perforated sheet. Then the membrane is applied and held in place at specific pressure and cured. If UV is used for curing, then the sheet and or the membrane must be transparent to the UV light. Although epoxy is discussed in this disclosure, most adhesives (silicone based, acrylic based, etc.) will work as described above as long as they are compatible with the rigid sheet, membrane and assay.

3. Solvent- A solvent that dissolves the perforated sheets only is applied to 1 surface of the perforated sheet or to the membrane. The membrane is pressed onto the perforated sheet and held until the excess solvent has been dispersed. The dissolved resin will be pushed into the pores of the membrane. In another method, a solvent that can dissolve both the perforated sheet and the membrane is applied only to the perforated sheet. The membrane is pressed onto the perforated sheet and held until the excess solvent has been dispersed. In this method the dissolved resin from the membrane and the dissolved resin from the perforated sheet mix and solidify. For example, Durapore® membrane produced by Millipore Corporation, would be solvent bonded to a polycarbonate sheet with methylene chloride. It is critical that the solvent be compatible with the materials used to produce the support and the membrane.

4. Non-contact fusion bonding- The surface of the perforated sheet is heated to it's melting point. The heat source is quickly removed and the membrane is pressed and held until the resin solidifies.

5. Diffusion bonding- The membrane and perforated sheet are pressed together at a "critical" temperature and pressure. At the critical point the resins will molecularly mix and solidify.

The present invention also provides a process of making a multi well membrane with limited cross talk. Specifically the process further comprises the step of making the seal formed around the individual wells after the lamination step impervious to the filtrate.

In applications where filtrate collection is not required, the seal between the support and the membrane needs only to be secure enough to prevent the membrane from releasing from the sheet and prevent the fluid from crossing from well to well between the sheet and the surface of the membrane. In applications that require filtrate collection, it is imperative that the seal formed around the individual wells is impervious to the filtrate so that cross talk between the wells is avoided.

The present invention provides a variety of different means of making the seal formed around the individual wells after the lamination step impervious to the filtrate.

1) Collapsing the pores in the membrane with heat and prior to laminating to the support. Collapsing the pores could possibly be done at the same time as laminating.

2) After laminating, break or remove membrane from between the wells by die cutting, ultrasonic vibration or heat.

3) Using a hydrophobic barrier pre or post laminating.

4) Filling the non-well forming membrane pores with epoxy.

5) Using solvents that will solvate the sheet and the membrane, thereby collapsing the pores in non-well forming membrane.

6) Using solvents that will dissolve only the rigid sheet. This will fill the pores in the non well-forming membrane with material from the rigid sheet.

The Sectional View of Figure 1 presents the use of an underdrain 20 with present invention. Underdrains are typically vacuum formed or molded and may be added after the membrane has been laminated it may added at same time as the membrane. The same bonding technologies described above would be used during lamination of the underdrain 20.

The present invention results in a superior multi-well membrane device process because the manufacturing cost thereof on a well-to-well basis will be much less expensive than prior art because the support or rigid sheet will be less expensive than a molded part.

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The present invention results in a superior multi-well membrane device process because the assembly process could be a web converting process. Use of such process would further reduce assembly costs.

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The present invention results in a superior multi-well membrane device process because multiple resins and thickness are readily available for the rigid sheets. Moreover, product design variations (chemical compatibilities, geometries, thicknesses and the like) can be made with minor die punch changes (this cannot be done with injection molds) and minor adjustments to the assembly equipment.

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The present invention results in a superior multi-well membrane device process because the rigid sheet concept allows for multiple line extensions using the same assembly equipment.

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The present invention results in a superior multi-well membrane device because it provides substantially increased well density, lower volume, tailored volume in a single card and the ability to use PTFE on a cost effective basis.

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The above examples are not to be construed as limiting the scope of the subject invention, which is set forth in the claims below. Those of ordinary skill in the art will appreciate the types of membranes appropriate to practice the present invention.

## CLAIMS

1. A multi-well membrane filter, the filter comprising:  
a support characterized by through holes not having been molded therein; and a membrane filter fixed to said support so at least one side of at least two such through holes are covered such that the device has at least two wells suitable for receiving material to be assayed.
2. The multi-well membrane filter of claim 1, wherein the support includes glass.
3. The multi-well membrane filter of claim 1, wherein the support includes metallic materials.
4. The multi-well membrane filter of claim 1, wherein the support includes ceramic materials.
5. The multi-well membrane filter of claim 1, wherein the support includes elastomeric materials.
6. The multi-well membrane filter of claim 1, wherein the support includes coated cellulosic materials.
7. The multi-well membrane filter of claim 1, wherein the support includes a polymeric material.
8. The multi-well membrane filter of claim 2, wherein the polymeric material includes polyethylene.
9. The multi-well membrane filter of claim 2, wherein the polymeric material includes acrylic.

10. The multi-well membrane filter of claim 2, wherein the polymeric material includes PTFE.
11. The multi-well membrane filter of claim 2, wherein the polymeric material includes polycarbonate.
12. The multi-well membrane filter of claim 2, wherein the polymeric material includes styrene.
13. The multi-well membrane filter of claim 1, wherein the support and membrane are configured to have at least 96 wells.
14. The multi-well membrane filter of claim 13, wherein the support and membrane are configured to have at least 384 wells.
15. The multi-well membrane filter of claim 1, wherein at least two wells have different volumes.
16. The multi-well membrane filter of claims 1 and 14, wherein the volume of each well is in the range of 50 to 150 microliters.
17. The multi-well membrane filter of claim 16, wherein the volume of each well is in the range of 70 to 130 microliters.
18. The multi-well membrane filter of claim 1, wherein at least two cells have different shapes.
19. The multi-well membrane filter of claim 1 further comprising an underdrain laminated to the opposite side of the membrane.
20. The multi-well membrane filter of claim 1, wherein the membrane contains patterned porous structures.

21. A method of producing a multi-well membrane filter device, the method comprising:
- selecting a pre-formed support suitable for affixing a membrane thereto;
  - removing material from such pre-formed support so as to form substantially aligned through holes therein;
  - selecting a membrane suitable for filtering solutions in a laboratory setting; and
  - forming wells by laminating the membrane to the support.
22. The method of claim 21 further comprising extruding a material to form the pre-formed support.
23. The method of claim 21, wherein material is removed from the pre-formed support by selectively drilling out material to be removed.
24. The method of claim 21, wherein material is removed from the pre-formed support by selectively punching out material to be removed.
25. The method of claim 21, wherein material is removed from the pre-formed support by selectively burning material to be removed.
26. The method of claim 21, wherein material is removed from the pre-formed support by selectively dissolving material to be removed.
27. The method of claim 21, wherein the membrane is laminated to the support in a web converting process.
28. The method of claim 21, wherein the membrane is laminated to the support by diffusion bonding.
29. The method of claim 21, wherein the membrane is laminated to the support by adhesive bonding.

30. The method of claim 21, wherein the membrane is laminated to the support by welding.
31. The method of claim 21, wherein the membrane is laminated to the support by thermal bonding.
32. The method of claim 21 further comprising the step of making the seal formed around the individual wells after the lamination step impervious to the filtrate.

PCT/US00/25585  
MILLIPORE CORPORATION

New Claims 33 to 45

33. A method of producing a multi-well membrane filter device, comprising the steps of:

selecting a pre-formed individual or continuous support sheet of a predetermined thickness;

selectively forming through holes corresponding to a desired well configuration and in a desired well matrix array into the support sheet by a material removing process;

attaching a filter membrane by a laminating process to one side of the support sheet provided with the through holes.

34. The method of claim 33, comprising the step of extruding a material to form the pre-formed individual support sheet.

35. The method of claim 33, comprising the step of maintaining the support sheet as continuous web during the steps of forming the through holes and attaching the filter membrane and subsequently cutting the device to a desired size.

36. The method of claim 33, 34 or 35, wherein the material removing process applied in the step of selectively forming the through holes into the support sheet is one selected of the following: drilling, punching, burning, dissolving.

37. The method of any one of claims 33 to 36, wherein the laminating process for attaching the filter membrane to the support sheet is one selected of the following: a web converting process, diffusion bonding, adhesive bonding, welding, thermal bonding.



38. The method of any one of claims 33 to 37, comprising the step of making the areas of the filter membrane around the individual through holes impervious to a filtrate, wherein this step is performed after, immediately before or simultaneously with the attaching step.

39. The method of claim 38, wherein the step of making the areas of the filter membrane around the individual through holes impervious to a filtrate is one selected of the following: collapsing pores in the filter membrane, breaking or removing filter membrane, applying a hydrophobic barrier, filling membrane pores with epoxy.

40. The method of any one of claims 33 to 39, comprising the step of laminating an underdrain layer to the outer surface of the filter membrane.

41. The method of any one of claims 33 to 40, wherein the pre-formed individual or continuous support sheet is selected from the following materials: glass, metallic materials, ceramic materials, elastomeric materials, coated cellulosic materials, polymeric materials.

42. The method of claim 41, wherein the polymeric material for the pre-formed individual or continuous support sheet includes: polyethylene, acrylic, PTFE, polycarbonate, styrene.

43. The method of any one of claims 33 to 42, wherein a volume of the wells defined by the configuration of the through holes and the thickness of the support sheet is in the range of 50 to 150 microliters, preferably in the range of 70 to 130 microliters.

44. The method of any one of claims 33 to 43, wherein at least two of the through holes on a filter device have different configurations.

45. The method of any one of claims 33 to 44, wherein the well array of a filter device comprises at least 96 wells, preferably at least 384 wells.

2025-03-03 10:00:00

(19) World Intellectual Property Organization  
International Bureau



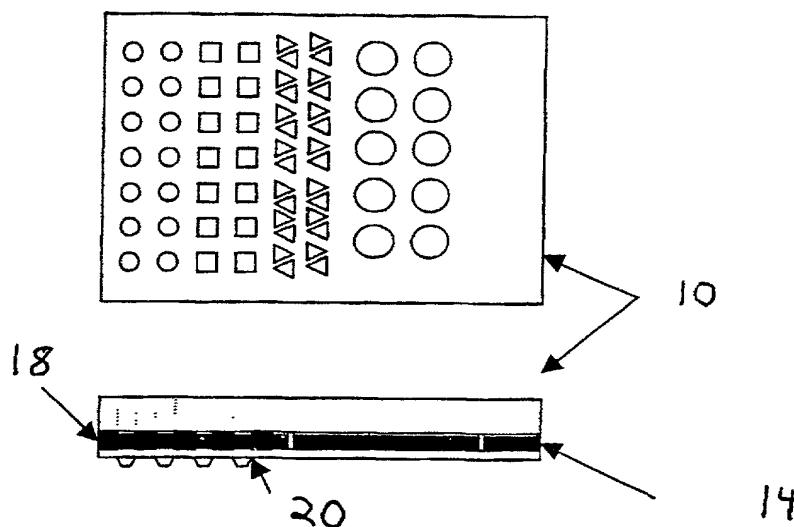
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22 March 2001 (22.03.2001)

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(10) International Publication Number  
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(75) Inventor/Applicant (for US only): **FOLEY, Brian**  
(21) International Application Number: **PCT/US00/25585** [US/US]; 53 Vince Brook Road, Westford, MA 01886 (US).  
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(71) Applicant (for all designated States except US): **MILLIPORE CORPORATION** [US/US]; King, Timothy, J., 80 Ashby Road, Bedford, MA 01730 (US). For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **HIGH THROUGHPUT SCREENING CARD**



(57) Abstract: The present invention provides multi-well membrane filter and methods of producing same, the multi-well membrane filter comprising a non-injection molded support and filter membrane laminated thereto, the method particularly adapted for producing multi-well membrane filters that have a substantial well density and small volume sample wells.

4354001

WO 01/19502 A2

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains valid OMB control number.

**DECLARATION FOR UTILITY OR****DESIGN****PATENT APPLICATION**☐ Declaration

Submitted

OR

☐ Declaration

Submitted after Initial

with Initial

Filing (surcharge

Filing

(37 CFR 1.16(e))  
Required)

Attorney Docket No.

MCA-483 PC/US

First Named Inventor

Brian Foley

COMPLETE IF KNOWN

Application Number

Not yet assigned

Filing Date

Group Art Unit

Not yet assigned

Examiner Name

Not yet assigned

As a below named inventor, I hereby declare that:

My residence, mailing address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled.

HIGH THROUGHPUT SCREEN CARD

(Title of the Invention)

the specification of which

☐ is attached hereto

OR

☒ was filed on (MM/DD/YYYY)

September 18, 2000

as United States Application Number or PCT International

Application Number

PCT/US00/25585

and was amended on (MM/DD/YYYY)

(if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT International filing date of the continuation-in-part application.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or (f), or 365(b) of any foreign application(s) for patent, inventor's or plant breeder's rights certificate(s), or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent, inventor's or plant breeder's rights certificate(s), or any PCT international application having a filing date before that of the application on which priority is claimed

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached?	
				YES	NO
PCT/US00/25585	PCT	09/18/2000	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
			<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

☐ Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

Application Number(s)	Filing Date (MM/DD/YYYY)	
		<input type="checkbox"/> Additional provisional application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

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Burden Hour Statement: This form is estimated to take 21 minutes to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS, SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

**DECLARATION – Utility or Design Patent Application**

Direct all correspondence to:

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

**NAME OF SOLE OR FIRST INVENTOR:**☐ A petition has been filed for this unsigned inventor

Given Name

Brian

Family Name

FOLEY

(first and middle [if any])

or Surname

Inventor's

Signature

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2/6/02

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**NAME OF SECOND INVENTOR:**☐ A petition has been filed for this unsigned inventor

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(first and middle [if any])

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or Surname

Inventor's

Signature

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☐ Additional inventors are being named on the \_\_\_\_ supplemental Additional Inventor(s) sheet(s) PTO/SB/02A attached hereto.